In the Claims

Claims 1-179 (canceled)

Claim 180 (currently amended):

A method of identifying crystalline salts of a small molecule pharmaceutical using a system comprising a series of integrated modules, or workstations, comprising:

(a) preparing and identifying an array of at least 96 samples in tubes and support plates or in sample well plates using an automated dispensing apparatus directed by a work list generated by formulation software, said work list allowing a file to be used as a process command rather than discrete programmed steps, and dispensing components into sample tubes or sample wells with a sample generation module, wherein each sample contains less than about 100 milligrams of said small molecule pharmaceutical, and each sample differs with respect to at least one of:

(i) the amount or concentration of the small molecule pharmaceutical;

(ii) an identity of one or more of a solvent, acid or base; or

(iii) an amount or concentration of one or more of a solvent, acid or base;

(b) sealing said samples;

(c) processing said samples comprising heating said samples in a sample incubation module to a temperature (T1), analyzing said samples for the presence of undissolved solids using visual analysis, cooling said samples to a final temperature (T2), wherein at least one of the processed samples comprises a crystalline salt form of the small molecule pharmaceutical;

(d) analyzing the processed array of samples comprising detecting crystalline solid formation in said samples using visual analysis, measuring a property for each crystalline solid and using the results of said measuring to group similar crystalline salt polymorphs, hydrates and solvates that belong to the same crystal family using informatics.

Claim 181 (previously presented):

The method of claim 180, comprising the further analysis of at least one representative of each crystal family and any orphan crystals.

Claim 182 (previously presented):

The method of claim 180, comprising the addition of said samples to tubes in a support plate.

Claim 183 (previously presented):

The method of claim 182, wherein said tubes are glass tubes and said support plate is a metal support plate.

Claim 184 (previously presented):

The method of claim 182, comprising sealing said tubes with a cap.

Claim 185 (previously presented):

The method of claim 180, wherein said array comprises at least 1000 samples.

Claim 186 (previously presented):

The method of claim 180, further comprising the generation of a work list for instructing an automated distribution mechanism to prepare said array of samples.

Claim 187 (previously presented):

The method of claim 180, comprising the dispensing of components by a liquid handling system with pipette tips having septum-piercing capability.

Claim 188 (previously presented):

The method of claim 180, wherein said sample contains less than 1 milligram of said small molecule pharmaceutical.

Claim 189 (previously presented):

The method of claim 180, wherein said samples are grouped using Raman spectroscopy.

Claim 190 (previously presented):

The method of claim 180, wherein said processing further comprises the quenching of the crystallization process by removing solvent from the samples.

Claim 191 (previously presented):

The method of claim 180, wherein said processing further comprises adding a non-solvent to said samples.

Claim 192 (previously presented):

The method of claim 180, wherein said processing further comprises evaporating solvent from said samples.

Claim 193 (previously presented):

The method of claim 184, comprising the piercing of said cap and aspiration of fluid from said samples.

Claim 194 (previously presented):

The method of claim 180, comprising analyzing said array of samples with a polarized light filter apparatus.

Claim 195 (previously presented):

The method of claim 180, wherein the small molecule pharmaceutical has previously evaded crystallization.

Claim 196 (previously presented):

The method of claim 180, wherein the crystalline salt identified in said processed samples is an additional polymorph of small molecule pharmaceutical previously known as a monomorphic compound.

Claim 197 (previously presented):

The method of claim 180, wherein said visual analysis is used as a filtering means to reduce the numbers of samples that will ultimately undergo in-depth analysis.

Claim 198 (previously presented):

The method of claim 180, wherein said grouped samples comprise a category selected from the group consisting of: a) samples containing no precipitate; b) samples with a single polymorph; c) samples with a polymorph mixture; d) samples with amorphous forms of said small molecule pharmaceutical; and e) samples with mixtures of categories b-d.

Claim 199 (currently amended):

The method of claim 180, further comprising analyzing said samples for at least one additional property, wherein said property is a chemical, structural or physical property.

Claim 200 (previously presented):

The method of claim 180, wherein said small molecule pharmaceutical is a known compound.

Claim 201 (previously presented):

The method of claim 180, wherein said small molecule pharmaceutical is an unknown compound.

Claim 202 (previously presented):

The method of claim 180, wherein said array comprises at least 1 sub-array.

Claim 203 (previously presented):

The method of claim 180, wherein said array comprises at least 1 sub-array with at least 24 samples.

Claim 204 (previously presented):

The method of claim 180, wherein an individual sample within said array is subjected to processing methods that are different from the processing methods to which another sample is subjected.

Claim 205 (previously presented):

The method of claim 204, wherein said individual sample is subjected to processing methods comprising adjusting the solvent removal rate.

Claim 206 (previously presented):

The method of claim 204, wherein said individual sample is subjected to processing methods comprising introducing a nucleation event.

Claim 207 (previously presented):

The method of claim 204, wherein said individual sample is subjected to processing methods comprising adding one or more additional components.

Claim 208 (previously presented):

The method of claim 204, wherein said individual sample is subjected to processing methods comprising introducing a precipitation event.

Claim 209 (previously presented):

The method of claim 204, wherein said individual sample is subjected to processing methods comprising adjusting the solvent composition.

Claim 210 (previously presented):

The method of claim 204, wherein said individual sample is subjected to processing methods comprising adjusting or controlling evaporation of the solvent.

Claim 211 (previously presented):

The method of claim 204, wherein said individual sample is subjected to processing methods comprising adding a non-solvent.

Claim 212 (previously presented):

The method of claim 180, wherein said array comprises sub-arrays, and wherein an individual sample within a sub-array is subjected to processing methods that are different from the processing methods to which another sample within the sub-array is subjected.

Claim 213 (previously presented):

The method of claim 212, wherein said individual sample is subjected to processing methods comprising adjusting the solvent removal rate.

Claim 214 (previously presented):

The method of claim 212, wherein said individual sample is subjected to processing methods comprising introducing a nucleation event.

Claim 215 (previously presented):

The method of claim 212, wherein said individual sample is subjected to processing methods comprising adding one or more additional components.

Claim 216 (previously presented):

The method of claim 212, wherein said individual sample is subjected to processing methods comprising introducing a precipitation event.

Claim 217 (previously presented):

The method of claim 212, wherein said individual sample is subjected to processing methods comprising adjusting the solvent composition.

Claim 218 (previously presented):

The method of claim 212, wherein said individual sample is subjected to processing methods comprising adjusting or controlling evaporation of the solvent.

Claim 219 (previously presented):

The method of claim 212, wherein said individual sample is subjected to processing methods comprising adding a non-solvent.

Claim 220 (previously presented):

The method of claim 180, wherein said array comprises sub-arrays, and wherein an individual sub-array is subjected to processing methods that are different from the processing methods to which another sub-array is subjected.

Claim 221 (previously presented):

The method of claim 220, wherein said individual sub-array is subjected to processing methods comprising adjusting the solvent removal rate.

Claim 222 (previously presented):

The method of claim 220, wherein said individual sub-array is subjected to processing methods comprising introducing a nucleation event.

Claim 223 (previously presented):

The method of claim 220, wherein said individual sub-array is subjected to processing methods comprising adding one or more additional components.

Claim 224 (previously presented):

The method of claim 220, wherein said individual sub-array is subjected to processing methods comprising introducing a precipitation event.

Claim 225 (previously presented):

The method of claim 220, wherein said individual sub-array is subjected to processing methods comprising adjusting the solvent composition.

Claim 226 (previously presented):

The method of claim 220, wherein said individual sub-array is subjected to processing methods comprising adjusting or controlling evaporation of the solvent.

Claim 227 (previously presented):

The method of claim 220, wherein said individual sub-array is subjected to processing methods comprising adding a non-solvent.

Claim 228 (previously presented):

The method of claim 180, wherein said small molecule pharmaceutical has a molecular weight less than about 1000 g/mol.

Claim 229 (previously presented):

The method of claim 180, wherein the amount of said small molecule pharmaceutical in each sample is less than about 1 milligram.

Claim 230 (previously presented):

The method of claim 180, wherein the amount of said small molecule pharmaceutical in each sample is less than about 100 micrograms.

Claim 231 (previously presented):

The method of claim 180, wherein the amount of said small molecule pharmaceutical in each sample is less than about 100 nanograms.

Claim 232 (previously presented):

The method of claim 180, wherein the total volume of each sample is between 100-250 μl.

Claim 233 (previously presented):

The method of claim 184, wherein said cap can be pierced with a standard syringe needle and fluid aspirated through the syringe tip to remove solvent from the sample.

Claim 234 (previously presented):

The method of claim 180, wherein one or more samples differ from one or more other samples with respect to the amount or concentration of the small molecule pharmaceutical.

Claim 235 (previously presented):

The method of claim 180, wherein one or more samples differ from one or more other samples with respect to the identity of one or more of a solvent.

Claim 236 (previously presented):

The method of claim 180, wherein said small molecule pharmaceutical is added to a series of different solvents ranging in polarity from extremely polar to non-polar.

Claim 237 (previously presented):

The method of claim 180, wherein mixed solvents are used to change the thermodynamic activity of one of the solvents independent of temperature.

Claim 238 (previously presented):

The method of claim 180, wherein one or more samples differ from one or more other samples with respect to the amount or concentration of one or more of an acid.

Claim 239 (previously presented):

The method of claim 238, wherein said one or more of an acid are those that form succinate, chloride, malate, or stearate salts with a basic compound.

Claim 240 (previously presented):

The method of claim 238, wherein said acid are those that form maleate, citrate, tartrate, or mesylate salts with a basic compound.

Claim 241 (previously presented):

The method of claim 238, wherein said acid are those that form succinate, acetate, chloride or mesylate salts with a basic compound.

Claim 242 (previously presented):

The method of claim 238, wherein said acid are those that form chloride, malate, maleate, or mesylate salts with a basic compound.

Claim 243 (previously presented):

The method of claim 238, wherein said acid are those that form succinate, stearate, citrate or tartrate salts with a basic compound.

Claim 244 (previously presented):

The method of claim 238, wherein said acid are those that form acetate, succinate, mesylate or stearate salts with a basic compound.

Claim 245 (previously presented):

The method of claim 238, wherein said acid are those that form benzenesulfonate, malate, mesylate or succinate salts with a basic compound.

Claim 246 (previously presented):

The method of claim 180, wherein one or more samples differ from one or more other samples with respect to the identity of one or more of a base.

Claim 247 (previously presented):

The method of claim 180, wherein said components comprise an additive that affects particle or crystal size.

Claim 248 (previously presented):

The method of claim 180, wherein said components comprise an additive that affects crystal habit.

Claim 249 (previously presented):

The method of claim 180, wherein said components comprise an additive that affects polymorphic form.

Claim 250 (previously presented):

The method of claim 180, wherein said components comprise an additive that promotes or controls nucleation.

Claim 251 (previously presented):

The method of claim 180, wherein said components comprise an additive that affects growth rate of a specific crystal.

Claim 252 (previously presented):

The method of claim 180, wherein said components comprise an additive that dissolves solid-forms.

Claim 253 (previously presented):

The method of claim 180, wherein said components comprise an additive that inhibits crystallization or precipitation.

Claim 254 (previously presented):

The method of claim 180, wherein said components comprise an additive that is a reaction by product.

Claim 255 (previously presented):

The method of claim 180, wherein said processed samples comprise two or more different polymorphs of the small molecule pharmaceutical.

Claim 256 (previously presented):

The method of claim 180, wherein said processed samples comprise two or more crystalline forms of the small molecule pharmaceutical, and wherein said crystalline forms have a different crystal habit.

Claim 257 (currently amended):

The method of ~~claim 200~~claim 199, wherein the physical property screened is physical stability.

Claim 258 (currently amended):

The method of ~~claim 200~~claim 199, wherein the physical property screened is solubility.

Claim 259 (currently amended):

The method of ~~claim 200~~claim 199, wherein the physical property screened is dissolution.

Claim 260 (currently amended):

The method of ~~claim 200~~claim 199, wherein the physical property screened is compressibility.

Claim 261 (currently amended):

The method of ~~claim 180~~claim 199, wherein the physical property screened is compactibility.

Claim 262 (currently amended):

The method of ~~claim 200~~claim 199, wherein the physical property screened is melting point.

Claim 263 (currently amended):

The method of ~~claim 200~~claim 199, wherein the physical property screened is resistance to absorption of ambient moisture.

Claim 264 (currently amended):

The method of ~~claim 200~~claim 199, wherein the physical property screened is bioavailability.

Claim 265 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is surface to volume ratio.

Claim 266 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is degree of agglomeration.

Claim 267 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is porosity.

Claim 268 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is particle size.

Claim 269 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is particle size distribution.

Claim 270 (currently amended):

The method of ~~claim 200~~claim 199, wherein the chemical property screened is chemical stability.

Claim 271 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is resistance to chemical reactions induced by heat.

Claim 272 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is resistance to chemical reactions induced by ultraviolet light.

Claim 273 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is resistance to chemical reactions induced by moisture.

Claim 274 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is resistance to chemical reactions between components.

Claim 275 (currently amended):

The method of ~~claim 200~~claim 199, wherein the structural property screened is resistance to chemical reactions induced by oxygen.

Claim 276 (previously presented):

The method of claim 180, wherein the processed samples are analyzed by machine vision technology.

Claim 277 (previously presented):

The method of claim 180, wherein the processed samples are analyzed by video-optical microscopy.

Claim 278 (previously presented):

The method of claim 180, wherein the processed samples are analyzed by image analysis.

Claim 279 (previously presented):

The method of claim 189, wherein the processed samples are analyzed by polarized light analysis.

Claim 280 (previously presented):

The method of claim 180, wherein the processed samples are analyzed by near field scanning optical microscopy.

Claim 281 (previously presented):

The method of claim 180, wherein the processed samples are analyzed by far field scanning optical microscopy.

Claim 282 (previously presented):

The method of claim 180, wherein the processed samples are analyzed by atomic-force microscopy.

Claim 283 (previously presented):

The method of claim 180, wherein the processed samples are analyzed by micro-thermal analysis.

Claim 284 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by infrared spectroscopy.

Claim 285 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by near infrared spectroscopy.

Claim 286 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by Raman spectroscopy.

Claim 287 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by NMR.

Claim 288 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by x-ray diffraction.

Claim 289 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by neutron diffraction.

Claim 290 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by powder x-ray diffraction.

Claim 291 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by light microscopy.

Claim 292 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by second harmonic generation.

Claim 293 (previously presented):

The method of claim 180, comprising analyzing the crystalline salt form by electron microscopy.

Claim 294 (previously presented):

The method of claim 180, wherein the processed samples are analyzed by an in vitro assay.

Claim 295 (previously presented):

The method of claim 180, wherein said crystalline salt form is a solvate.

Claim 296 (previously presented):

The method of claim 180, wherein said crystalline salt form is a desolvated solvate.

Claim 297 (previously presented):

The method of claim 180, wherein said crystalline salt form is, a clathrate.

Claim 298 (previously presented):

The method of claim 180, wherein said crystalline salt form is an inclusion.

Claim 299 (previously presented):

The method of claim 180, wherein said system comprises a sample incubation and sample detection module.

Claim 300 (previously presented):

The method of claim 180, wherein data collected is used to identify occurrence of conditions that define occurrence domains that will give rise to a specific crystal form.

Claim 301 (previously presented):

The method of claim 189, wherein said visual analysis comprises machine vision technology.

Claim 302 (currently amended):

A method of identifying crystalline salts of a small molecule pharmaceutical using a system comprising a series of integrated modules, or workstations, comprising:

(a) preparing and identifying an array of at least 96 samples in tubes and support plates or in sample well plates using an automated dispensing apparatus directed by a work list generated by formulation software, said work list allowing a file to be used as a process command rather than discrete programmed steps, and dispensing components into sample tubes or sample wells with a sample generation module, wherein each sample contains less than about 100 milligrams of said small molecule pharmaceutical, one or more of a solvent, and each sample differs with respect to at least one of:

(i) the amount or concentration of the small molecule pharmaceutical;

(ii) an amount, concentration or identity of said one or more of a solvent; or

(iii) an amount, concentration or identity of one or more of an acid or base;

(b) sealing said samples;

(c) processing said samples comprising evaporating solvent from said samples wherein at least one of the processed samples comprises a crystalline salt form of the small molecule pharmaceutical;

(d) analyzing the processed array of samples comprising detecting crystalline solid formation in said samples using visual analysis, measuring a property for each crystalline solid and using the results of said measuring to group similar crystalline salt polymorphs, hydrates and solvates that belong to the same crystal family using informatics.

Claim 303 (currently amended):

A method of identifying crystalline salts of a small molecule pharmaceutical using a system comprising a series of integrated modules, or workstations, comprising:

(a) preparing and identifying an array of at least 96 samples in tubes and support plates or in sample well plates using an automated dispensing apparatus directed by a work list generated by formulation software, said work list allowing a file to be used as a process command rather than discrete programmed steps, and dispensing components into sample tubes or sample wells with a sample generation module, wherein each sample contains less than about 100 milligrams of said small molecule pharmaceutical, and each sample differs with respect to at least one of:

(i) the amount or concentration of the small molecule pharmaceutical;

(ii) an identity of one or more of a solvent, acid or base; or

(iii) an amount or concentration of one or more of a solvent, acid or base;

(b) sealing said samples;

(c) processing said samples comprising adding an antisolvent to said samples wherein at least one of the processed samples comprises a crystalline salt form of the small molecule pharmaceutical;

(d) analyzing the processed array of samples comprising detecting crystalline solid formation in said samples using visual analysis, measuring a property for each crystalline

solid and using the results of said measuring to group similar crystalline salt polymorphs, hydrates and solvates that belong to the same crystal family using informatics.

Claim 304 (currently amended):

A method of identifying crystalline salts of a small molecule pharmaceutical comprising:

(a) preparing and identifying an array of at least 96 samples in tubes and support plates or in sample well plates using an automated dispensing apparatus directed by a work list generated by formulation software, said work list allowing a file to be used as a process command rather than discrete programmed steps, and dispensing: i) said small molecule pharmaceutical; a salt forming component; and additional components into sample tubes or sample wells with a sample generation module, wherein said array comprises at least 1 group of at least 24 samples, each sample contains less than about 100 milligrams of said small molecule pharmaceutical, and each sample differs with respect to at least one of:

(i) the amount or concentration of the small molecule pharmaceutical;

(ii) an identity of one or more of a solvent, acid or base; or

(iii) an amount or concentration of one or more of a solvent, acid or base;

(b) sealing said samples;

(c) processing said samples comprising heating said samples in a sample incubation module to a temperature (T1), analyzing said samples for the presence of undissolved solids using visual analysis, cooling said samples to a final temperature (T2), wherein at least one of the processed samples comprises a crystalline salt form of the small molecule pharmaceutical; and

(d) analyzing the processed array of samples comprising detecting crystalline solid formation in said samples using visual analysis, measuring a property for each crystalline solid and using the results of said measuring to group similar crystalline salt polymorphs, hydrates and solvates that belong to the same crystal family using informatics.